

# **EXHIBIT S**

# ALLERGIC DISEASES

Diagnosis and Management

Second Edition

EDITED BY

**M.D.**  
Dy Professor  
Immunology  
Chairman  
of Medicine  
University, Chicago  
Contributors



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EDITED BY

**ROY PATTERSON, M.D.**

*Ernest S. Bazley Professor  
Chief, Section of Allergy and Immunology  
Chairman*

*Department of Medicine  
Northwestern University, Chicago  
With 28 Contributors*

*In Memory of  
Ernest S. Bazley*

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The authors and publishers have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

**DONALD W.**  
*Assistant  
Attending  
Active St*

**BERNARD HE**  
*Clinical*

**WALTER W. C**  
*Chock-Pa  
Assistant  
Honolulu*

**LLOYD CRAW**  
*Clinical F  
Center fo*

**RICHARD D.**  
*Clinical  
Allergist*

**RICHARD D.**  
*Assistant  
Sciences;*

**ANGELO E. F.**  
*Associate  
Attending*

**JORDAN N. F.**  
*Professor*

**JAMES E. FIFE**  
*Assistant  
Baltimore,  
Former As*

**THOMAS M. C**  
*Assistant  
Colorado*

## VASOMOTOR RHINITIS 197

There is no adequate or laboratory method of indicating to the patient how long immunotherapy must be continued. There are no long-term clinical studies of how patients fare after variable years of therapy. Therefore, the clinical response to therapy dictates the decision concerning the duration of specific treatment. It is recommended that a minimum of three years of immunotherapy be given in an effort to avoid the rapid recurrence of symptoms in uncomplicated allergic rhinitis. In those who have persisting complications such as polyps, sinusitis, otitis media, and so forth, it may be indicated to continue therapy somewhat longer since clinical improvement may take longer in such patients. A detailed discussion of the therapeutic and practical aspects of immunotherapy can be found in Chapter 11.

## VASOMOTOR RHINITIS

## Definition

Vasomotor rhinitis is a disease of unknown etiology. It is associated with an altered vasomotor control of the nose resulting in the development of chronic nasal congestion. Many physicians use the term *vasomotor rhinitis* as a descriptive one to include both nonseasonal, perennial allergic, and the nonallergic forms of rhinitis. In this discussion, the use of the term *vasomotor rhinitis* is restricted to the nonimmunologic, noninfectious, chronic type of rhinitis.

## Pathophysiology

The nasal mucous membrane has a rich blood supply which is under the control of the autonomic nervous system. The blood supply derived from branches of the ophthalmic, maxillary, and facial arteries form an extensive subepithelial plexus of arterioles. Blood drains from the internal nose via a very rich superficial venous plexus, forming cavernous spaces that resemble those found in erectile tissue. Autonomic nerves controlling this vascular bed travel with the sensory nerves in the area, the maxillary division of the fifth cranial nerve. Parasympathetic function originates in the superior salivatory nucleus, and reaches the nose through the vidian nerve and sphenopalatine ganglion. Cervical sympathetic branches from the carotid nerves join the vidian nerve to distribute to the nose.

Many nonspecific stimuli act on the autonomic nerves, resulting in reflex changes in the nasal mucosa, in particular that covering the turbinates, where the venous plexus is especially abundant. Emotional stimuli have been shown to trigger nasal obstruction and rhinorrhea.<sup>25</sup> In addition, rapid changes in body temperature and alterations in humidity may induce similar nasal changes in susceptible patients.<sup>54</sup> Horner's syndrome, in which the cervical sympathetic nerves are ablated, is associated with unilateral nasal obstruction and overactivity of the mucous glands. By altering laminar air flow, a deviated nasal septum may induce reflex changes in the nasal mucosa, leading to the development or aggravation of vasomotor rhinitis. Although the exact mechanism is not known, endocrine factors may be important causes in some patients with vasomotor rhinitis. Pregnancy, menstruation, menopause, and marked hypothyroidism may be accompanied by the symptoms of a nonallergic chronic rhinitis.

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**Clinical Features**

Patients with vasomotor rhinitis complain of chronic nasal congestion, rhinorrhea, and sneezing. Frequently, they describe the nasal blockage as alternating from side to side. No seasonal absence of symptoms is noted, although during the summer, when temperatures are more constant, the symptoms may be less than in the winter. The symptoms do not change significantly in relationship to any geographic changes. In patients with vasomotor rhinitis, no definite allergic or infectious factors can be shown to be clinically important. Physical factors and psychologic stresses may trigger nasal symptoms. The symptoms may be worse on awakening in the morning. Sudden changes in body temperature, exposure to drafts, high humidity, chemical fumes, tobacco smoke, and emotional upsets are common nonspecific stimuli that precipitate or aggravate the nasal symptoms in susceptible patients. In vasomotor rhinitis of pregnancy, symptoms appear late in the first or second trimester, and disappear shortly after parturition. Occasionally, birth control pills, which essentially induce a pseudo-pregnant condition, may cause vasomotor rhinitis.

Examination of the nose usually reveals marked edema resulting in nasal obstruction. The nasal mucosa generally appears erythematous, but occasionally may appear pale. The nasal secretions are usually mucoid, and only rarely does the stained nasal smear reveal the presence of significant numbers of eosinophils. Most patients with vasomotor rhinitis show no reactions to skin tests. In a small proportion of individuals, skin tests may be positive but do not correlate with the clinical history and are coincidental. Nasal polyps frequently complicate long-standing vasomotor rhinitis and add to the nasal obstruction. The important features of allergic rhinitis and vasomotor rhinitis are compared in Table 7-3.

**Treatment**

Therapy consists of symptomatic treatment with antihistamines and oral nasal decongestants, and avoidance of precipitating factors. Thyroid replacement therapy will diminish the nasal symptoms associated with hypothyroidism. Discontinuing the use of oral contraceptive pills will alleviate the nasal symptoms in the occasional patient in whom they induce vasomotor rhinitis. Surgical correction of a deviated nasal septum is indicated in those with an associated marked nasal obstruction. The patient with vasomotor rhinitis of

**TABLE 7-3. Comparison of Allergic Versus Vasomotor (Nonallergic) Rhinitis**

	Allergic	Vasomotor
Seasonal variation	Yes	No
Nasal, ocular, or palatal itching	Yes	Rarely
Rhinorrhea	Watery	Mucoid
Pale nasal mucosa	Almost always	Not common
Nasal polyps	Occasionally	Occasionally
Collateral allergy	Common	Unusual (coincidental)
Family history of allergy	Usual	Coincidental
Nasal secretion eosinophil smear	Usually positive	Rarely positive
Skin test reactivity	Almost always positive	Coincidental

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